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EXAMINER

NIEBAUER, RONALD T

ART UNIT

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1654

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/584,874	<b>Applicant(s)</b> BENATTI ET AL.	
	<b>Examiner</b> RONALD T. NIEBAUER	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15 and 17-28 is/are pending in the application.
- 4a) Of the above claim(s) 19-22 and 24-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15, 17-18, 23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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### **DETAILED ACTION**

Applicants amendments and arguments filed 10/9/08 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

As discussed previously, Applicants elected with traverse Group I (claims 15-18,23) and the species where R is H (see claim 15).

Claims 1-14,16 have been cancelled. Claims 15,18 have been amended. As discussed previously the elected species was found to be obvious based on the prior art.

Claims 19-22,24-28 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 3/12/08.

Claims 15,17-18,23 are under consideration.

### ***Claim Rejections - 35 USC § 103***

Claims were rejected previously under 103 using the references cited below. Since the claims have been amended the rejection has been updated.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 15,17-18,23** are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 5,464,825) and McMurry (Organic Chemistry 4th edition 1996, page 825).

Anderson teach methods for increasing glutathione (GSH) levels or levels of glutathione equivalents (column 3 lines 22-23). Anderson specifically recites N-acyl glutathiones as a type of glutathione derivative (column 3 line 24). Anderson teaches that the acyl group can contain 1 to 9 carbon atoms and is preferably 1 to 4 carbon atoms, for example propyl (column 3 lines 33-37). Anderson teach that acylated esters are de-esterified in the cell (column 3 line 29,67). Anderson teach that elevated GSH levels are desired in the treatment of viral infections (column 3 lines 11-18).

Anderson specifically teach compounds identified as N-acetyl GSH monoesters (column 4 lines line 10-30). Anderson specifically teach that the R1 is preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). Anderson teach that the compounds are hydrolyzed (column 4 line 21) to form N-acyl GSH which is the de-esterified compound. Anderson teach pharmaceuticals of such compounds (column 4 lines 30-32). Anderson does not expressly show

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the reaction scheme of the hydrolysis reaction. McMurry (bottom of page 825) teach that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson (column 4 line 21) includes a carboxylic acid not an ester.

Neither of the references expressly teach the compound of the instant invention.

Anderson specifically teach compounds identified as N-acetyl GSH monoesters (column 4 lines line 10-30). Anderson specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. For example R1 can be methyl, ethyl, or propyl. When R1 is propyl and the compound is de-esterified (column 3 line 29,67) or hydrolyzed (column 4 line 21) as described by Anderson the resulting product is a carboxylic acid that is identical to the elected species of claim 15 of the instant invention where R is H (the elected species). Thus the limitations of claims 15 are met.

In other words, the disclosure of 'N-acyl GSH' (column 4 line 21) includes various compounds that have been hydrolyzed. Since Anderson teach such compounds as pharmaceuticals (column 4 line 30-32), teach carriers (column 5 lines 23-30) and teach applications for treatment of viral infections (column 2 line 11-18) the limitations of claims 17-18,23 are met.

It has been recently held that "obvious to try" may be an appropriate test under 103 KSR v. Teleflex, 550 U.S. \_\_\_, 82 USPQ2d 1385, 1389 (2007). The Supreme Court stated in KSR

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When there is motivation

"to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, \_\_\_, 82 USPQ2d 1385, 1397 (2007).

In the instant case, the claims would have been obvious because 'a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense'. In particular, Anderson recognize the need for increasing GSH cellular levels (column 2-3) and teach a finite number of compounds to be used (column 4 line 10-30). Further, Anderson specifically teach R1 values and teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that the compound with R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. Further, such compounds are described as being de-esterified and hydrolyzed. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

### ***Response to Arguments 103 rejection***

Since the claims have been amended, a new rejection adapted to the claims is recited above using the same references as in the previous rejection.

Applicants argue that the present claims do not recite an ester group on the glycine residue but require a carboxyl group and that the art teach the monoester.

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Applicants argue that the prior art does not teach that the compound could enhance intracellular GSH levels and does not teach a difference between R1 groups of different lengths.

Applicants argue that there is an unexpected result and the applicant assert a certain hydrocarbon length is preferred.

Applicants argue that de-esterification is no more than a theory.

Applicants argue that case law states that it remains necessary to identify a reason to modify a compound.

Applicants argue that the prior art provides no reasonable expectation of success.

Applicant's arguments filed 10/9/08 have been fully considered but they are not persuasive.

Although Applicants argue that the present claims do not recite an ester group on the glycine residue but require a carboxyl group and that the art teach the monoester, as discussed previously Anderson teach that the monoester is hydrolyzed to form N-acyl GSH which is shown schematically in column 4 lines 18-24. McMurry (bottom of page 825) teach that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson (column 4 line 21) includes a carboxylic acid not an ester. Thus, in addition to the ester Anderson also teach the hydrolyzed form.

Although Applicants argue that the prior art does not teach that the compound could enhance intracellular GSH levels and does not teach a difference between R1 groups of different lengths, it is noted that the instant claims are drawn to products not to methods of determining differences between R1 groups of different lengths. Since the references render the claims

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obvious the claim limitations are met since the same compound would have the same properties.

Further, section 2144.09 of the MPEP (last paragraph) states:

‘However, a claimed compound may be obvious because it was suggested by, or structurally similar to, a prior art compound even though a particular benefit of the claimed compound asserted by patentee is not expressly disclosed in the prior art. It is the differences in fact in their respective properties which are determinative of nonobviousness. If the prior art compound does in fact possess a particular benefit, even though the benefit is not recognized in the prior art, applicant’s recognition of the benefit is not in itself sufficient to distinguish the claimed compound from the prior art. In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).’ In the instant case, the prior art suggests that the monoester can be converted via hydrolysis to the carboxylic acid (column 4 lines 18-24). Further, Anderson specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48).

Although Applicants argue that there is an unexpected result and the applicant assert a certain hydrocarbon length is preferred, it is noted that Anderson specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). Further, it is noted that an affidavit or declaration must compare the claimed subject matter with the closest prior art to be effective to rebut a prima facie case of obviousness (see MPEP section 716.02(e)) and the burden is on the applicant to establish that the results are unexpected and significant (MPEP section 716.02(b)). In the instant case, the prior art (Anderson) teach the compounds for treatment of viral infections (column 3 lines 16-18) and teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48).



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Although Applicants argue that de-esterification is no more than a theory, Anderson teach that the monoester is hydrolyzed to form N-acyl GSH which is shown schematically in column 4 lines 18-24. McMurry (bottom of page 825) teach that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson (column 4 line 21) includes a carboxylic acid not an ester. Thus, in addition to the ester Anderson also teach the hydrolyzed form. As such, one would recognize the hydrolysis reaction as set forth by McMurry (page 825 last paragraph) as a fact, not a theory.

Although Applicants argue that case law states that it remains necessary to identify a reason to modify a compound, the instant claims would have been obvious because 'a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense'. In particular, Anderson recognize the need for increasing GSH cellular levels (column 2-3) and teach a finite number of compounds to be used (column 4 line 10-30). Further, Anderson specifically teach R1 values and teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that the compound with R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. Further, such compounds are described as being de-esterified and hydrolyzed.

Although Applicants argue that the prior art provides no reasonable expectation of success, Anderson teach that the invention is used to increase GSH levels in treatment of viral infections for example (column 3 lines 11-17). Further, Anderson specifically teach R1 values

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and teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that the compound with R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. Further, such compounds are described as being de-esterified and hydrolyzed.

### ***Conclusion***

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/  
Primary Examiner, Art Unit 1654

/Ronald T Niebauer/  
Examiner, Art Unit 1654